

# Epidemiology of Hypertension as a Public Health Problem: An Overview as Background for Evaluation of Blood Lead-Blood Pressure Relationship

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An overview of the epidemiology of blood pressure is presented as background for the International Symposium of Blood Lead-Blood Pressure Relationships. The correlates of blood pressure distributions in populations are varied and numerous. They have to be considered as either potential confounders or modifiers of any blood pressure-blood lead relationship detected. The relation of blood pressure to cardiovascular morbidity and mortality emphasizes the importance of detecting and elucidating any possible causal association of blood lead with blood pressure at low levels. The task of this symposium is of public health importance, as relatively minor changes in the distribution and mean levels of blood pressure in populations are associated with major morbidity and mortality consequences.

## Introduction

This symposium is addressed to a review of the evidence that there is a relationship between blood lead and blood pressure levels. We have organized presentations that permit discussion and evaluation of published investigations and work in progress relating to both human and animal studies. The human studies are further stratified as clinical, occupational epidemiologic, and general population epidemiologic studies. Most controversy in this field has been engendered by the general population studies, which have suggested a causal relationship between increases in blood lead levels within the range of values lower than those considered clinically significant and increases in blood pressure, also within the range below values considered clinically significant as hypertensive. The association has not been found in all studies and, when present, has been such that increase in blood pressure with increase in blood lead levels has been of small absolute magnitude and not constant across age, sex, and race subgroups. Despite the seemingly small elevations in blood pressure when viewed from the clinical perspective of each individual, the potential

public health importance of a blood lead relationship is considerable due to the strong association of blood pressure with cardiovascular morbidity and mortality, the leading cause(s) of death in our society, and the large number of individuals exposed. Evaluation of the possible contribution of blood lead levels to these outcomes from observational epidemiologic studies requires assessment of whether there is evidence of an association of blood lead with blood pressure levels, its strength, dose-response nature, consistency across studies, freedom from measurement biases, and statistical independence from the effects of confounding influences. Finally, the biologic and pathophysiologic plausibility of the epidemiologic observational association is to be assessed in light of the human and animal experimental studies.

As background for the specific studies to be reviewed at the symposium, it was deemed appropriate to present an overview of some of the elements of the epidemiology of blood pressure relevant to the blood lead-blood pressure issue. Selectivity was necessary in choosing from a vast literature, an epidemiologic literature whose summarizations themselves have been extensive (1-4). The guiding principle in choosing material was to illuminate methodologic and substantive issues that could misinform studies of blood pressure in relation to blood lead levels. Particular

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attention is called to the continuous distribution of blood pressure levels in populations; the large number and varied nature of correlates of blood pressure; the continuous nature of the cardiovascular morbidity and mortality risk functions associated with increasing blood pressure; and the resulting large potential population disease burden of increases in blood pressure, seemingly clinically insignificant for each individual.

## Distribution of Blood Pressure in Populations

Blood pressure is difficult to measure reliably in population studies. There is marked intraindividual variability in response to the physical and social environmental circumstances of measurement and psychologic responses to the measuring situation. Although there are experiments suggesting an influence of lead on pressure responsivity, there are no large epidemiologic studies addressing this issue.

Observer sources of measurement variation are considerable and require training, standardization, and quality control assessment to assure comparability among observers within a given study. Unfortunately, objective methods to assure measurement comparability across studies, or over time within study populations, have not been satisfactorily developed for large epidemiologic studies. Although follow-up studies over long periods of time demonstrate some tracking of individuals (i.e., maintenance of rank position based on blood pressure level), and one casual blood pressure level is predictive of morbidity and mortality, these associations are increased by assessments repeated and averaged over time. Thus, there are methodologic problems in evaluating population changes in blood pressure over time, problems of moment given changes in blood lead over time.

The result of all sources of variation of blood pressure measurements within and among individuals in populations is a continuous distribution, unimodal in nature, without any clear dividing points permitting level *per se* to distinguish the normotensive from the categorical (arbitrarily defined) hypertensive. In the epidemiologic domain the population is the unit of study, not the individual, and populations differ in the distribution of blood pressure. They differ both in the mean level and in the amount of variation around the mean. Generally, but not invariably, there is increasing variance and increasing skewness towards higher values with increasing mean levels of blood pressure. On comparison of two populations with different mean levels, the proportion of individuals with high levels gets progressively more dissimilar between the populations as one moves further out to higher values (arbitrarily categorized as hypertensive) in the tails of the distributions. Thus, seemingly small differences in mean values of blood pressure of populations can be accompanied by sizable differences

in proportions of individuals with elevated values or alternatively expressed, sizable differences in proportions of hypertensives.

## Correlates of Blood Pressure Levels in Populations

The known correlates of blood pressure levels in populations are large in number, and thereby the potential for confounding of a blood pressure relationship with another attribute, such as blood lead levels, is commensurately large. In addition to the large number of correlates of blood pressure levels in populations, their operation at different levels of bio-social organization increases the complexity of assessing their possible confounding or effect modification of a blood lead-blood pressure relationship. A brief consideration of some of these correlates is organized by the following categories: demographic, familial, physical environment, social environment, and behavioral factors.

### Demographic Correlates

The trends in blood pressure with age, among the most important factors in the etiology of hypertension, and the association of hypertension with sex are often considered invariable biological effects, minimally amenable to modification; however, age and sex may be surrogate indicators of social and physiochemical environmental processes. For example, although most populations show increases in mean blood pressure levels with age, some do not. The common characteristics of populations without evidence of increase in blood pressure with age have variously been identified as absence of industrialization, persistence of traditional social structures, and low sodium ingestion.

Populations can be classified by the rate of change of blood pressure with age and the level of blood pressure. At one extreme are populations with low levels of blood pressure and no increase of mean pressure with age; at an opposite extreme are populations with high levels and marked increase in blood pressure with increasing age, e.g., rural southern U.S. blacks.

Although linear increase in pressure with age is an appropriate approximation of most population observations for systolic blood pressure, the cross-sectional diastolic blood pressure data are more accurately represented by a curvilinear relationship to age, with mean diastolic pressure reaching a plateau in middle age and decreasing at older ages. The mean blood pressure of different aged individuals in cross-sectional surveys are single point-in-time values for different individuals at different achieved ages, and therefore represent the composite effects, if any, of aging *per se*, different experiences of different birth cohorts, and selective survival. Prospective studies in industrialized societies confirm the average rise in blood pressure (particularly systolic) with age observed in

cross-sectional surveys; however, not all individuals experience the rise, and, among those who do, there is considerable variation in the rate of rise.

Mean blood pressure levels and the prevalence of hypertension vary with sex in a manner that differs with age epochs. Comparison in industrialized societies of studies of children younger than age 14 reveals no consistent sex differences; in adolescence, young adulthood, and through age 45 there is unanimity among reported studies of higher mean blood pressure levels in males and a male excess in the prevalence of hypertension; a cross-over then occurs in these cross-sectional surveys at about age 45, after which mean blood pressure becomes higher in women than in men.

Among the most consistent findings in the epidemiology of hypertension is an excess in its frequency and deleterious sequelae in adult black populations in the United States. Numerous studies have reported a shift in the distribution of blood pressure levels in blacks toward higher values for both sexes at all adult ages. The age at which blacks first manifest higher blood pressure than whites is not clear. Studies of teenagers have been approximately equally divided, with some showing and some not showing black-white differences in blood pressure distribution.

Although it is not clear at what age the black-white difference is first manifest, there is uniformity among studies in finding higher blood pressure levels and an excess of end organ sequelae associated with hypertension from young adulthood on, in surveys of blacks sampled from national prevalence surveys and surveys of local communities. The higher blood lead levels in blacks invites the hypothesis that at least some of the shift toward higher blood pressure distributions in blacks is attributable to lead exposure.

## Genetic and Family Aggregation

There is a large body of empirical data indicating similarity of blood pressure levels within families. Briefly summarized, first degree genetic relatives of all ages from infancy to old age, studied in diverse social and cultural settings, tend to resemble one another in levels of systolic and diastolic blood pressure. The similarity of blood pressure levels of relatives does not argue unequivocally for a genetic cause. In addition to sharing genes, relatives share common physical, social, and psychological environments, which can influence blood pressure. Aggregation of blood pressure levels among nongenetically related household members, including but not restricted to spouse pairs, has been reported in some studies. Greater similarity would be expected among age-contemporaneous sibling pairs than intergenerational parent-offspring pairs, based on both environmental and genetic hypotheses. The empirical findings are in conflict; about half of the reported studies show higher similarity in sibling pairs. The measure of similarity of blood pressure among genetic relatives is greater than that

observed among spouses or other nongenetic related household members, in the instances where the latter do demonstrate significant similarity of blood pressure levels. As measured by the correlation coefficient, this is greater for monozygotic than for dizygotic twins, greater for first degree genetic relatives than spouse pairs, and greater among family members with natural than adopted children. These findings are consistent with genetic factors influencing blood pressure within populations.

These studies neither clarify nor delineate the relative importance of genetic and familial environmental factors, nor the nature of the genetic mechanisms. The possibility that lead exerts a different blood pressure-elevating effect among genetically different susceptibles has not been empirically tested.

## Social and Physical Environment

The sensitivity of blood pressure regulatory mechanisms to acute psychological stimuli and strong emotional reactions is marked. Neurohumoral blood pressure and cardiovascular control is an integral component in normal hemodynamics and adaptation to sudden environmental challenges. Therefore, a wide variety of interpersonal experiences, external situations, emotions, and perceived and expected changes in life situations is associated with acute elevation of blood pressure. These psychophysiological responses are part of the normal repertoire of responses. Psychosocial theories of hypertension suggest that such factors are also involved in the etiology of sustained hypertension. Neurohumoral relations to a wide range of processes influencing blood pressure have been postulated, extending from the personality basis of altered blood pressure reactivity of the individual to the social origins of increased stressors, incorporating both acquired, learned modes of response and inborn constitutional predisposition.

In most developed societies, social stratification, whether indexed by achieved education, occupational status, income level, or a combination of these measures, has been found to be inversely associated with blood pressure. This has been observed in the U.S. for both whites and blacks. For example, among the more than 150,000 individuals screened for the Hypertension Detection and Follow-Up Program, there was a stepwise increase in the prevalence of categorically defined hypertension with decreasing educational achievement for both whites and blacks. Much of the education-blood pressure association was explained by an increase in the prevalence of obesity with decreasing education.

The association of blood lead levels with social status and the social environment, i.e., higher lead levels among the poor and among those residing in more highly exposed rural and urban places of residence, requires consideration of these circumstances in the study of processes relating blood lead to blood pressure.

Numerous elements in the food, water, air, and soil

of the ambient physical environment and in the workplace are related to blood pressure. Among the elements most studied and quantitatively most important are sodium, potassium, calcium, and magnesium. Complex interactions among these elements with blood pressure and their possible role(s) in any lead-blood pressure association require systematic investigations.

## Behavior and Obesity

A sizable correlation between blood pressure and indices of body weight in relation to height in children and adults has repeatedly been demonstrated in both cross-sectional and longitudinal population-based studies. The relationships are continuous across the range of blood pressure levels.

In addition to measurements of the association between blood pressure and overweight as continuous traits, quantitative estimates have been derived from the relation between baseline weight, weight gain, and the incidence of hypertension, classified categorically.

Individual behavior is a strong determinant of blood pressure levels in populations. The balance of dietary caloric intake and caloric expenditure by physical activity is reflected in weight and obesity, major correlates of blood pressure, and its distribution in communities. Obesity *per se* is probably related to blood pressure; not just the amount, but the bodily regional distribution of fat appears to be associated with elevated blood pressure. Accumulation in the abdominal area contrasted with the extremity areas seems to have stronger association not just with blood pressure, but also with other cardiovascular risk factors. Dietary fat intake, the ratio of saturated to unsaturated fat, and the possibility that the fat content of marine animals influence blood pressure levels are under intensive investigation at present. Relationships have been observed in population-based studies between the amount of alcohol consumed and average blood pressure levels. Smoking represents an area of considerable controversy in that several studies have found an inverse association between smoking and blood pressure, but most investigators attribute that to the lower weight of smokers. The increment in weight on cessation of smoking is associated with an increase in blood pressure.

The possibility of confounding of the blood lead-blood pressure association by the behavioral, dietary, alcohol consumption, and smoking attributes discussed requires detailed attention and analysis.

## Consequences of Blood Pressure Levels in Populations

Given the overview presentation of the distribution and antecedents, we can now turn our attention to some of the consequences of blood pressure levels in populations. Numerous studies have documented the

relation of blood pressure to morbidity and mortality; one is a recent study based on the screening of more than 300,000 men for the Multiple Risk Factor Intervention Trial and the subsequent 6-year follow-up for coronary heart disease mortality. Blood pressures were stratified into age-specific quintiles, and there generally was a monotonic increase in coronary mortality with increasing levels of blood pressure in each age group. There was, however, a suggestion of a J-shaped curve in the oldest age stratum, with the lowest quintile group of blood pressures having slightly higher mortality. Although this risk function shape has been observed in the Framingham study and other studies, this is a controversial area; in general, the relationship found is of a monotonically increasing nature. Comparing the within-age group risk of mortality of those in the highest quintile to those in the lowest quintile shows a consistent decrease in the relative risk with increasing age. In contrast, attributable risk, i.e., the arithmetic difference in the rates between those in the highest and lowest quintile, shows a stepwise, consistent increase with increasing age.

Elevated blood pressure is a risk factor not only for coronary disease, but also for more specifically pressure-related conditions such as congestive heart failure and strokes. The relative risk for the pressure-related phenomena, particularly for stroke, is markedly higher than for coronary disease: somewhat more than 2 for coronary and 10 for stroke.

An estimation of the population impact is assessed by considering the continuous distribution of blood pressure levels in populations, the risk function of stepwise increases in disease frequency with increasing levels of blood pressure, and the excess risk associated with elevated levels above arbitrarily chosen cut points. Most of the excess disease in populations is associated with what clinically would be considered relatively mild to moderate elevations of blood pressure. Although the relative risk increases markedly with progression to higher levels of blood pressure, the prevalence in the population of individuals with mild to moderate hypertension is proportionately greater. The net effect is that most of the excess morbidity and mortality is associated with clinically relatively minor increases in the mid-portion of the range of distribution of blood pressure. This is an important consideration for this symposium. The proportion of all the disease in a given population associated with elevated blood pressure is the product of the attributable risk and the prevalence of elevated pressure at any chosen level and is called the population attributable risk. In the instance of mortality, if one divides the population attributable risk by all cause mortality, the quotient is the population attributable fraction; namely, the proportion of all mortality in the community associated with elevated pressures. As studied in one community-based study, Evans County, a very high proportion of all cause mortality (ranging from approximately 18% for white females to > 40% for black females) was associated with elevated blood pressure.

## Temporal and Spatial Variation in Hypertension-Related Mortality

Major temporal trends have been manifest for hypertension-related causes of death in the United States. After an earlier period of rise, coronary heart disease mortality rates have consistently shown an approximately 2% decline per year since mid-1960. There has been more than a 40% decline in coronary mortality in the last 20 years, reflected in all cardiovascular disease and in all-cause mortality rate declines. The decline started earlier and has been even greater for stroke mortality. In fact, stroke mortality started declining long before effective antihypertensive therapy was developed, so the determinants of declining stroke mortality clearly include factors other than medical treatment. However, since about 1972-73, coincidental with the initiation of a National High Blood Pressure Education Program in the U.S., there has been an acceleration of the decline in stroke mortality.

Many of the studies reviewed at this symposium have been performed during a period of sharply decreasing cardiovascular mortality. There also is marked geographic variation in the United States in stroke mortality. Most of the high rate areas are in the eastern portion of the United States; particularly, the *southeastern portion, and most of the low rate areas are in the western portion.* The geographic pattern, although decreasing, has persisted over the past 20 to 25 years, despite the marked decline in the level of mortality. Therefore, it is important to consider the possibility that there is geographic variation in blood pressure distributions and to account for this pos-

sibility in analyses of associations of blood pressure with blood lead using data derived from national samples.

## Conclusions

In summary, then, this paper has presented an overview of the correlates, antecedents, and determinants, which are extremely varied in kind and *numerous in amount, of blood pressure distributions* in populations. These factors have to be considered as either potential confounders or modifiers of any blood pressure-blood lead relationship detected. The relation of blood pressure to cardiovascular morbidity and mortality emphasizes the importance of detecting and elucidating any possible causal association of blood lead with blood pressure at low levels. The task of this symposium is of public health importance, as relatively minor changes in the distribution and mean levels of blood pressure in populations are associated with major morbidity and mortality consequences.

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